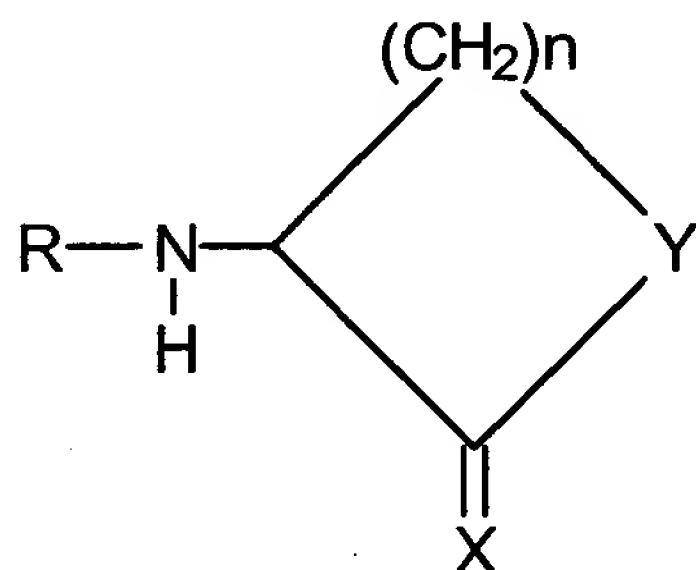


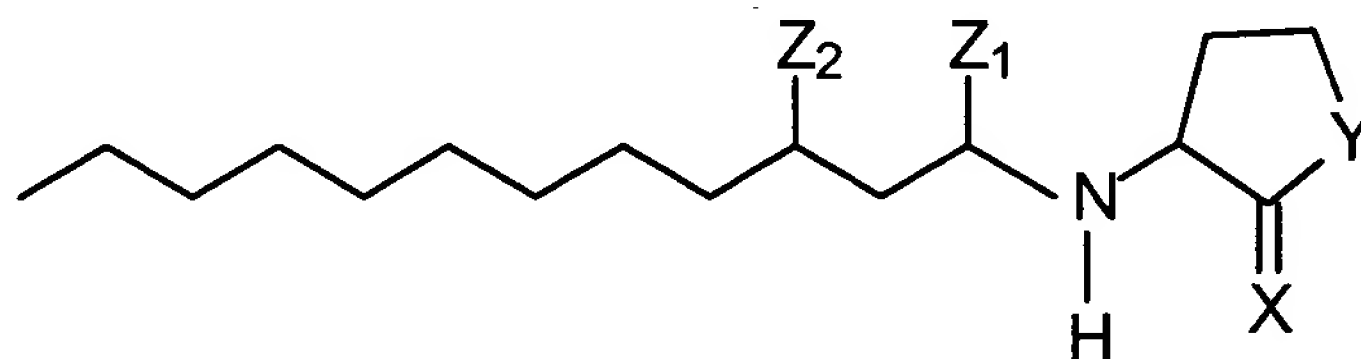
Amendments to the Specification:

Please amend the specification on page 2, lines 5-23 as follows:

The present invention is based, ~~at~~ least in part, on the discovery that the autoinducer molecule for *Pseudomonas aeruginosa* is N-(3-oxododecanoyl)homoserine lactone and not N-(β -ketocaproyl)homoserine lactone as previously believed. Upon the discovery of this novel autoinducer molecule, it was realized that autoinducer molecule(s) containing a fatty moiety or a moiety having at least seven members in the R moiety of the formula set forth below:



are involved in the regulation of gene expression. In the above formula, n is 2 or 3; Y is O, S, or NH; X is O, S, or NH; and R is a fatty hydrocarbon or acyl moiety that may be substituted or a moiety having at least seven members containing a ring structure that may be substituted. The present invention further pertains to ~~autoinducers~~ autoinducers molecules of the following formula:



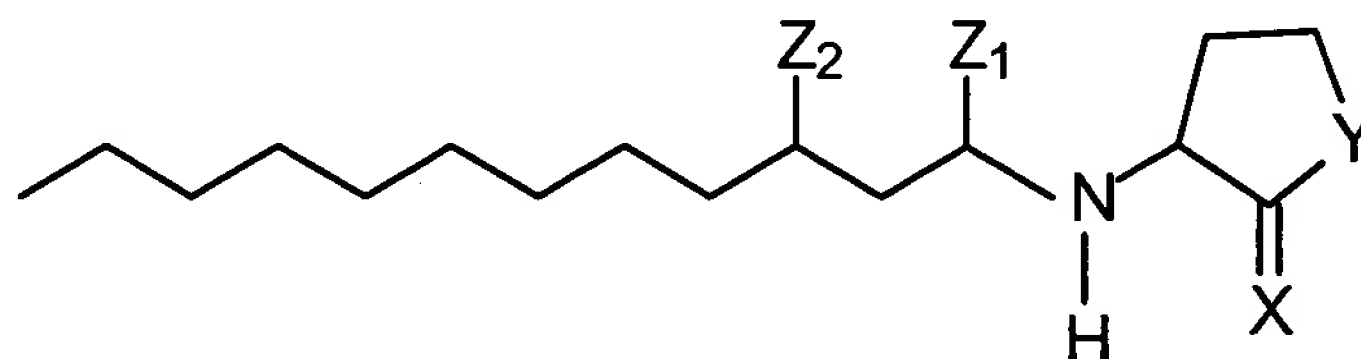
wherein X and Y are as defined above and Z_1 and Z_2 are independently selected from the group consisting of hydrogen, =O, =S, and =NH.

Please amend the specification on page 3, lines 15-23 as follows:

The present invention even further pertains to a method of inhibiting the infectivity of *Pseudomonas aeruginosa* and a method of treating an immunocompromised individual infected with *Pseudomonas aeruginosa*. Both of these methods involve the administration to an individual of a therapeutically effective amount of the agents and/or therapeutic compositions described above that inhibit the activity of the LasR protein and/or inhibit the autoinducer activity of N-(3-oxododecanoyl)homoserine lactone. An example of an immunocompromised individual ~~is~~ an individual afflicted with cystic fibrosis.

Please amend the specification on page 7, lines 18-23 as follows:

The present invention further pertains to ~~autoinducerautoinducer~~ molecules of the following formula:



wherein X and Y are as defined above and Z₁ and Z₂ are independently selected from the group consisting of hydrogen, =O, =S, and =NH.

Please amend the specification on page 10, lines 9-20 as follows:

The language "administering a therapeutically effective amount" is intended to include methods of giving or applying an agent to an organism which allow the agent to perform its intended therapeutic function. The therapeutically effective amounts of the agent will vary according to factors such as the degree of infection in the individual, the age, sex, and weight of the individual, and the ability of the agent to inhibit the activity of the LasR protein of *P. aeruginosa* in the individual. Dosage ~~regimens~~regimens can be adjusted to provide the optimum

therapeutic response. For example, several divided doses can be administered daily or the dose can be proportionally reduced as indicated by the exigencies of the therapeutic situation. Administering also includes contacting the agent with the LasR protein outside of an organism such as with a culture of bacteria.

Please amend the specification on page 10 line 32 to page 11 line 17 as follows:

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. In all cases, the composition must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid ~~polyethylenepolyethylene~~ glycol, and the like), suitable mixtures thereof, and vegetable oils. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Please amend the specification on page 17 line 22 to page 18 line 13 as follows:

The procedure for PAI purification was based on that described previously for purification of VAI (Eberhard, A., Burlingame, A.L., Eberhard, C., Kenyon, G.L., Nealson, K.H. and Oppenheimer, N.J. (1981) *Biochemistry* 20, 2444-2449). Cells and culture fluid were

separated by centrifugation (10,000 x g for 10 min. at 4°C). The culture fluid was then passed through a 0.2 µm pore-size filter, and the filtered material was extracted twice with equal volumes of ethyl acetate plus 0.1 ml/liter glacial acetic acid. The combined extracts were pooled, water was removed with magnesium sulfate, and the ethyl acetate was removed by rotary evaporation at 40-45°C. The residue was dissolved in 6 ml of ethyl acetate. The ethyl acetate was removed by rotary evaporation and the residue was then extracted with 5 ml of ethanol. The ethanol solution was ~~was~~ dried by rotary evaporation and the residue was dissolved in ethyl acetate. The ethyl acetate was removed and the residue was extracted in 5 ml of ethanol. This ethanol extract was dried, and dissolved in ethyl acetate. Finally, the sample was dried and dissolved in 0.2 ml of methanol. This sample was further purified by High Performance Liquid Chromatography (HPLC) with a C18 reverse phase column (0.46 x 25 cm). The *P. aeruginosa* autoinducer activity was first eluted as a sharp peak at 73 to 78% methanol in a linear 20 to 100% gradient of methanol and water. Fractions constituting this peak were pooled, dried by rotary evaporation and the residue dissolved in ethyl acetate plus acetic acid. The ethyl acetate was removed, the residue was dissolved in 0.1 ml of methanol and this solution was subjected to further purification by HPLC, eluting isocratically with 65% methanol in water. Fractions containing autoinducer activity were dried, dissolved in ethyl acetate plus acetic acid and stored at -20°C.

Please amend the first paragraph of the specification, previously amended on April 3, 2002, as follows:

This application is a continued prosecution application of serial no. 09/541873 filed on 4/3/00, now abandoned, which in turn is a continuation application of serial no. 08/456,864 filed on 3/17/99, and issued as U.S. Patent 6,057,288~~pending~~, which in turn is a continued prosecution application of 08/456,864 filed on 6/1/95, now abandoned, which in turn is a divisional application of serial no. 08/104,487 filed on August 9, 1993 and issued as U.S. Patent 5,591,872. The contents of all of the aforementioned application(s) are hereby incorporated by reference.